PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :
C08F 212/14, A01N 47/10
A01N 47/28, C07C 271/12
C07C 275/24

A1

(11) International Publication Number: WO 91/12282

(43) International Publication Date: 22 August 1991 (22.08.91)

(21) International Application Number: PCT/US91/00926

(22) International Filing Date: 12 February 1991 (12.02.91)

(30) Priority data:
479,840 14 February 1990 (14.02.90) US

(71) Applicant: H.B. FULLER LICENSING & FINANCING INC. [US/US]; 1100 North Market Street, Wilmington, DE 19890 (US).

(72) Inventor: OLSTEIN, Alan, D. ; 1841 Walsh Lane, Mendota Heights, MN 55118 (US).

(74) Agents: BYRNE, Linda, M. et al.; Merchant, Gould, Smith, Edell, Welter & Schmidt, 1000 Norwest Center, St. Paul, MN 55101 (US).

(81) Designated States: AT (European patent), BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: COPOLYMERS WITH INHERENT ANTIMICROBIAL ACTION

(57) Abstract

Polymeric materials employing quaternary compounds as biocidal agents are disclosed. The compounds may be copolymerized with vinyl monomers or used as an additive in latex, emulsion or adhesive systems.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**ES**	Spain	**MG**	Madagascar
AU	Australia	**FI**	Finland	**ML**	Mali
BB	Barbados	**FR**	France	**MN**	Mongolia
BE	Belgium	**GA**	Gabon	**MR**	Mauritania
BF	Burkina Faso	**GB**	United Kingdom	**MW**	Malawi
BG	Bulgaria	**GN**	Guinea	**NL**	Netherlands
BJ	Benin	**GR**	Greece	**NO**	Norway
BR	Brazil	**HU**	Hungary	**PL**	Poland
CA	Canada	**IT**	Italy	**RO**	Romania
CF	Central African Republic	**JP**	Japan	**SD**	Sudan
CG	Congo	**KP**	Democratic People's Republic of Korea	**SE**	Sweden
CH	Switzerland			**SN**	Senegal
CI	Côte d'Ivoire	**KR**	Republic of Korea	**SU**	Soviet Union
CM	Cameroon	**LI**	Liechtenstein	**TD**	Chad
CS	Czechoslovakia	**LK**	Sri Lanka	**TG**	Togo
DE	Germany	**LU**	Luxembourg	**US**	United States of America
DK	Denmark	**MC**	Monaco		

COPOLYMERS WITH INHERENT ANTIMICROBIAL ACTION

Technical Field

This invention relates to copolymers with inherent antimicrobial activity that can be used in typical polymer applications. The invention further relates to an inherently antimicrobial polymer latex and particularly to adhesive emulsions containing such copolymers. It further relates to inherently antimicrobial films and fibers comprising such copolymers.

Background of the Invention

Many polymer compositions and articles formed of polymers require sanitizing, biocidal, or antimicrobial properties. Biocidal agents can be added to polymer compositions or articles to serve this function. However, a biocidal agent cannot always be used. Further, when used, the cost and the complexity of forming the film or fiber, adhesive composition, etc., with the antimicrobial can be prohibitive or detrimental to polymer properties.

Quaternary ammonium polymers are known to have biocidal properties. U.S. Patent No. 4,532,128 illustrates certain quaternary ammonium polymers useful as preservatives for opthalmic solutions, hair care products, and topical pharmaceutical products.

U.S. Patent No. 4,429,096 relates to quarternary amine carbamate or urea compounds. The compounds may be combined with acrylamide to yield oligomers used in water clarification, flocculation, and hair spray application.

The growth of a variety of organisms on surfaces and in bulk materials has been a problem for many years. Organisms taking the form of both unicellular and multi-cellular forms have caused infection in humans and other animals, spoilage of foods, caused chemical degradation of a variety of chemicals, and have fouled surfaces in marine environments. In many other areas, the growth of

unicellular and multi-cellular organisms has been a cause of substantial economic loss and operational difficulty.

In aqueous and other chemical systems, contamination with typically unicellular microorganisms can often degrade natural and synthetic polymers causing substantial reduction in the desirable physical and chemical properties of a number of feedstocks. In a variety of areas, the infection of skin surfaces or wounds can cause significant illness, fever, and potential loss of limbs or lives of affected individuals.

In the marine environment, a variety of typically multi-cellular organisms form on hard surfaces such as ships, pilings, wharfs, quays, drilling rigs, sea water inlets, screens, etc. Such multi-cellular organisms must be removed mechanically if significant growth occurs that interferes with the operation of the associated surfaces. Such surfaces can be treated with chemical biocides, however, such materials to date tend to be toxic in nature and release materials such as organtin or organo copper anti-fouling agents. Such agents are currently being discouraged in the domestic and world markets due to environmental reasons.

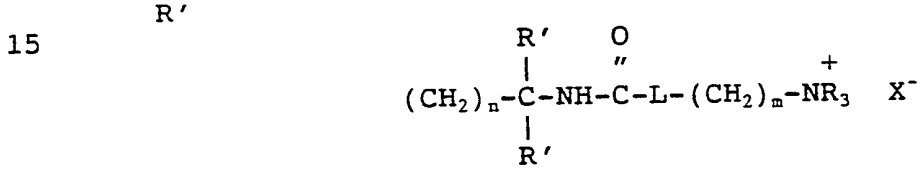
Compositions intended for the controlled release of a disinfectant from a film of stabilized hydrophilic polymer are disclosed in U.S. Pat. No. 3,966,902. The polymer complexes are stabilized as a metal complex by the addition of an inorganic aluminum, zirconium or zinc salt, such as aluminum chloride, to the polymerization mixture. The stabilization adjuvant is necessary because, upon contact with water, such films of simple hydrogels become highly swollen and rapidly elute their additives. Further, dry films, both simple and metal complexed hydrogels, do not adhere well to ceramic and other hard surfaces and can lose their adhesion completely when wetted.

Other antimicrobial agents have been combined with film-forming polymeric materials and have been used in the absence of a polymeric carrier. U.S. Pat. No. 3,325,436 discloses bacterial resistant latexes that incorporate alpha, alpha'-azobis(chloroformamadine). Similarly, U.S. Pat. No. 2,689,837 discloses polymeric vinyl halides having improved resistance to deterioration caused by fungal and bacterial attack, which incorporate copper 8-quinolinolate into the polymer. Also, U.S. Pat. No. 3,577,516 discloses a spray-on bandage material using acrylate or methacrylate polymers that may contain germicides or fungicides. Phenols and thiophenols are well-known antimicrobial agents and have been incorporated into polymeric compounds. U.S. Pat. No. 2,875,097 discloses the incorporation of phenolic compounds into polymers comprising heterocyclic nitrogen compounds. These polymers are typically used to render fabrics resistant to fungi and insect attack. U.S. Pat. No. 2,873,263 discloses an antibacterial polymeric resin used for fabricating plastic articles. These resins are formed by polymerizing an unsaturated monomer such as an alkyl acrylate in the presence of certain aromatic phenols or phenolic analogs.

The incorporation of various biocides into polymeric base material, either by physical entrapment, by ionic complexation or by copolymerization, has as yet not satisfactorily addressed the problem of providing polymeric compositions capable of forming adhesives, latexes or substrate materials that exhibit potent prolonged antimicrobial action without significant release of toxic materials. Therefore, a continuing need exists for an antimicrobial composition that can produce an ongoing biodegradable biocidal agent in sufficient concentration to provide a product substantially free of organisms.

Brief Description of the Invention

The invention provides a polymeric composition that yields biocidal polymers which may be incorporated into adhesives, latexes, fibers, fabrics, films, bulk polymer, etc. The biocidal polymer inherently prevents growth of organisms through the presence of strongly biocidal groups in the copolymer or by adding the biocidal copolymer to another polymer biological degradation and may also be used as an anti-fouling coating and in water treatment applications. The present invention provides an antimicrobial composition comprising a polymer made from a monomer having the active functional group according to the following general formula:



wherein L is -NH- or -O-; n is 0-6; m is 1-6; X^- is any inorganic or organic anion; each R′ is independently an H or C_{1-5} alkyl; each R is independently a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl, or a benzyl; and the molecular weight of the copolymer is at least about 20,000 weight average molecular weight. While the copolymer of the present invention may have a lower molecular weight, polymers having a weight of about 20,000 or greater provide preferable physical properties including viscosity, wetability when the polymer is used in solution, and osmotic responsiveness.

The polymeric material can be incorporated into an adhesive matrix, polymeric fibers, polymeric substrates, etc. Alternatively it may be used as an additive to adhesives, latexes, etc. When incorporated or added to polymers, the polymer displays biocidal properties.

Polymeric materials utilizing the biocide of the present invention can be a copolymer (a polymeric material having two or more monomer constituents), an oligopolymer (a relatively low molecular weight polymer), a terpolymer (a polymeric material having three or more monomers), etc.

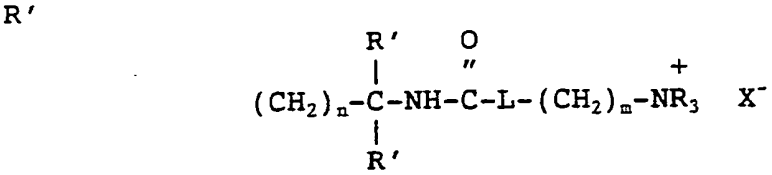
The invention also relates to a method of making polymeric substrates, polymeric compositions or any composition capable of receiving an additive as antimicrobial.

Detailed Description of the Invention

The present invention discloses polymeric materials that have incorporated therein monomers having an antimicrobial activity. The antimicrobial monomer may be polymerized into polymeric materials or antimicrobial polymers that may be added to other polymers. The instant antimicrobial composition can be used in polymeric matrices such as adhesives, lubricants, latexes, etc. The biocidal polymers of the present invention can be used in polymeric compositions that are often degraded by microrganisms or bacteria. The instant antimicrobial composition may be applied in a number of ways. Antimicrobial monomers can be copolymerized in an adhesive composition, latex composition, or materials such as fibers, films, adhesive substrates, etc., or may be incorporated in adhesives, latexes, etc., as an additive. Possible polymeric materials in which the present invention may be incorporated into are vinyls, polyesters, polycarbonates, and the like. When the antimicrobial is utilized as an additive, the antimicrobial may be used at a concentration of about 0.001 to about 1 wt-%.

Monomer

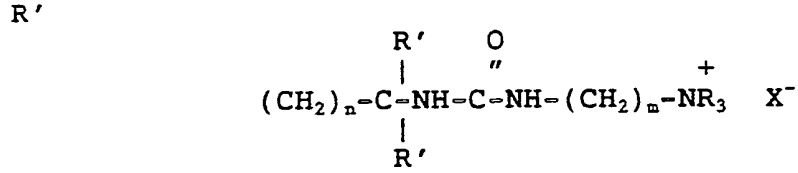
The monomeric materials used in preparing the biocidal polymers of the invention can be made by preparing a monomeric quaternary ammonium structure shown below.



wherein L is an -O- or an -NH-; n is 0-6; m is 1-6; X^- is any inorganic or organic anion; R′ is independently an H or C_{1-5} alkyl and R is a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl, or a benzyl. In the preferred compound, n=0, m=2 and at least two R substituents are methyl while the remaining R is C_{1-24}.

The above monomer is copolymerized with at least one other vinyl monomer. The quaternary monomer may comprise up to 99 mole percent of the copolymer, but has a preferred range of about 10-50 mole percent. The percentage of the antimicrobial monomer and other monomers will vary depending on the required antimicrobial activity, required physical and chemical polymer properties, costs, etc.

The synthesis of the present invention begins with the synthesis of the quaternary monomer compound below.



wherein n is equal to 0-6; m is equal to 1-6; X^- is any inorganic or organic anion; each R′ is independently an H or C_{1-5} alkyl, each R is independently a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl, or a benzyl, and the molecular weight of the monomer is at least about 20,000.

The quaternary amine monomer compounds of the invention are prepared by reacting a monoisocyanate compound with a quaternary ammonium compound having a group with a reactive hydrogen compound. The preferred monoisocyanate compound of the invention is the compound having a single

polymerizable vinyl group and a single mono isocyanate group. In preparation of the polymers of the invention, polymerization occurs through the vinyl group. The formation of the quaternary compound occurs by reaction between the isocyanate group and the active hydrogen of the quaternary compound. Preferred quaternary compounds comprise quaternary substituted alkanols and quaternary substituted alkyl amines. The hydroxyl group of the alcohol is reacted with the isocyanate group producing a carbamate linkage. The quaternary substituted amine compound is reacted with the isocyanate group producing a urea linkage.

Alternatively, the quaternary monomers of the invention can be prepared by reacting an isocyanate compound with a compound having an active hydrogen and amine functionality. That post reaction can be quaternized using conventional reactions. It is envisioned that amine functionality on the formed polymer material can be quaternized post polymerization. However, the preferred mode is to quaternize the amine prior to reaction with the isocyanate group or to quaternize the monomer after carbamate or urea formation.

The quaternary monomer compound can be polymerized with any number of comonomers to form either a latex or solution copolymer. The vinyl unsaturated monomer can be an alpha-olefin monomer such as ethylene, propylene, butylene, isobutylene, hexene; styrene, alpha methylstyrene, vinyl chloride, vinyl acetate, acrylonitrile, ricinoleic acid, oleic acid, linoleic acid, butadiene, and the like. Useful acrylic monomers include methacrylate, methylmethacrylate, hydroalkyl acrylate, hydroxy alkyl methacrylate, butyl acrylate, hexyl acrylate, cyclohexylacrylate, (2-hydroxyethyl) ethacrylate, (2- hydroxyethyl) ethacrylate, (2-hydroxyethyl) acrylate, (3-hydroxypropyl) ethacrylate,

(3-hydroxypropyl) acrylate, (3-hydroxypropyl) ethacrylate, (dimethylamino-ethyl) ethacrylate (pipiridinoethyl) methacrylate, (morpholinoethyl) methacrylate, and the like. Useful unsaturated dicarboxylic acids include itaconic acid, aconitic acid, cinnamic acid, crotonic acid, mesaconic acid, maleic acid, fumaric acid, and the like; alpha, beta unsaturated dicarboxylic acid esters of the dicarboxylic acid esters described above including aromatic esters, cycloalkyl esters, alkyl esters, hydroxy alkyl esters, alkoxy alkyl esters, and the like.

Vinyl heterocyclic monomers which are useful in the present invention include 2-vinyl pyrrolidone, n-vinyl pyridine, and vinyl epsilon captrolactam among others. As used herein, the term "cycloalkyl ester" includes mono, bi and tricycloalkyl esters and the term "aromatic ester" includes heteroaromatic esters.

Other useful comonomers include vinyl monomers having glycidyl or other epoxy functional groups. Also useful are comonomers such as γ-methacryloxypropyl trimethoxysilane, allyl trimethoxysilane, 2-allyl phenol, N-allyl morpholine, allyl glycidyl ether, allyl cinnamate, and allyl undecylenate among others. Other comonomers useful in the present invention include perfluoroalkyl acrylates such as 2,2,2 trifluoroethyl acrylate, and 1H, 1H, 11H eicrafluoroundecyl acylate. These monomers when polymerized with the quaternary monomer of the present invention are capable of preventing microfouling and macrofouling. This composition provides antifouling properties without the release of environmentally contaminating agents such as elemental tin or copper. This composition has the potential for eliminating the need for ship dry-docking altogether.

The copolymer of the present invention should generally have an average molecular weight of about 20,000 to 10

million with a preferred range of molecular weights falling in excess of 2 million.

The copolymers utilizing acrylamide of U.S. Patent No. 4,429,096 are not envisioned to be used with the present invention. In order for a copolymer of the quaternary amine compound of U.S. Patent No. 4,429,096 and acrylamide to be water soluble, useful in water clarification, and useful in hair sprays as described in the specification, molecular weights of the polymers has to remain fairly low.

Moreover, U.S. Patent No. 4,429,096 discloses polymers which, in their final form, are aqueous soluble acrylamide polymers incapable of becoming insoluble or emulsion polymers through radical reaction mechanisms.

In contrast, the polymers of the present invention are formed from monomers which are chemically reactive through radical mechanisms to form aqueous insoluble cross-linked antimicrobial materials. The resulting emulsified or dispersed polymers, in turn, are capable of forming a biologically active film on a chosen surface of deposition. The polymers of the present invention provide a mix of polar and nonpolar character which maintains the polymeric film on the surface of deposition and has a hydroscopic nature which facilitates the biocidal action of the polymer.

The proportions of each monomer can vary widely. The vinyl monomer may generally range from 1-99 mole percent and the monomer of the present invention may generally range from 1-99 mole percent, preferably from about 1 mole-% to 50 mole-% and most preferably from about 1-25 mole-% in latex polymer systems. In solution polymer systems the concentration of monomer of the present invention is substantially similar to that of latex polymers. However, the use of an organic solvent may tend to allow a greater concentration of active antimicrobial monomer. These molar

proportions will vary according to the necessary antimicrobial action desired, the economics of employing a large amount of antimicrobials, and the requirements of the physical properties of the polymers such as strength, melting point, etc.

The polymerization can be generally carried out in a closed vessel under heated conditions to form either a latex or solution polymers. Solution polymerization is generally carried out with the monomers in solution in an inert organic solvent such as tetrahydrofuran, methyl ethyl ketone, acetone, ethyl acetate, or other suitable solvents such as organic C_{2-4} alkanols. Organic solvents can also be mixed with compatible amounts of water in emulsion or inverse emulsion systems. Preferred solvents are nontoxic and odorless. Monomeric starting materials to form the biocidal polymers of the invention are typically dissolved or suspended in the solvent to a desired concentration. Preferably, the polymerization of the invention is typically performed at a concentration of about 12-60 wt-% of the monomers, preferably 2-25 wt-% of the monomers in the solvent material, although higher or lower concentrations may be employed depending on the given antimicrobial efficacy needed for any given application.

Polymerization reactions are typically initiated in a conventional manner, preferably by use of a suitable initiator. Examples of suitable initiators include 2,2'-azobis(2-methylpropanenitrile) (AIBN), dibenzoyl peroxide, tertiary butyl peroctoate cumene hydroperoxide, diisopropyl percarbonate, ammonium persulfate, and the like, per se, or in combination with a reducing agent in the form of an oxidation reduction catalyst system. During the course of the reaction, the reaction mixture may be agitated and heated preferably in an inert atmosphere (nitrogen, argon, etc.), to about 50-100°C., controlling the reaction

temperature to avoid destructive exotherms, preferably to about 75-95°C. After completion of the copolymerization reaction, the final product is purified to remove excess salts, amines and the like. Any known processes for isolating purifying polymers may be utilized. Some care should be taken to insure that no polymerization initiator remains in active form in the reaction mixture.

The molecular weight of the resulting polymer may vary. However, the molecular weight of the resulting copolymer is at least approximately 20,000. In the preferred embodiment, the molecular weight ranges from 20,000 to 10 million.

The monomer of the present invention may also be formulated into a latex polymer using an aqueous medium under substantially similar conditions to those used for solution polymerization. Also, while latex generally refers to polymers which are dispersed within an aqueous carrier these polymers may have partially soluble or completely soluble comonomer constituents. Depending on the comonomers used in the polymers of the present invention, these polymers form a dispersion of colloidal particles suspended in an aqueous carrier which, once dried, form an antimicrobially active film.

The possible uses of the present invention are many. The quaternary monomer in the present invention may be directly incorporated into polymeric film matrices, fibers, aqueous lattices, adhesives (both water-based and hot-melt), and may be used in anti-fouling coatings and water-treatment applications. Quaternary compounds may also be incorporated into the above systems as an additive.

In the present context, the monomer of the present invention may be used to prepare copolymers or grafted copolymers. Emulsion copolymers can be formed with the isocyanate-quaternary monomer of the present invention.

Comonomers including compounds such as styrene, and divinyl benzene among others can be used to make macroporous resins useful in the solid phase as disinfectants for water treatment.

The isocyanate-quaternary monomer of the present invention may also be copolymerized with urethane and acrylate type monomers to provide compositions useful as inhibiting corrosion in water base coatings and in powder coatings. The isocyanate-quaternary monomer of the present invention may also be copolymerized with acrylonitrile to create fibers useful in the formation of antimicrobial non-woven materials for application in areas such as hospital and medical environments. The isocyanate-quaternary monomer may also be used with comonomers such as quaternary monomers having epoxy functionalities to create resins useful as hard surface coatings in applications requiring environmental sanitization, sanitary paints, and as ionomeric adhesives. The isocyanate-quaternary monomer of the present invention may also be copolymerized through grafting methods well known to those of skill in the art. For instance, the isocyanate-quaternary monomer may be grafted to form acrylic emulsion latexes in application for the formation of self-preserving paints, adhesives, and environmental coatings. The isocyanate-quaternary monomer of the present invention may also be grafted onto cellulosic fibers again for the formation of non-woven compositions useful in medical and hospital environments among other areas. The isocyanate-quaternary monomer may also be grafted onto latex rubbers to provide antimicrobial elastic substrates which for example, may be used to provide medical disposables such as surgical gloves. The isocyanate-quaternary monomer may also be grafted onto nylon fibers to create membranes useful in the application of wound dressings as well as the creation of filter

materials which may be in turn used to provide highly pure pharmaceutical compositions.

The following examples illustrate the preparation of polymers utilizing the present invention in the preparation of films, fibers, aqueous lattices, and aqueous adhesives.

EXAMPLE 1

Hydroxylated dialkyl-methyl quaternary ammonium chloride was synthesized by dissolving. 168.8 g, 0.55 moles of methyldidecyl amine (DAMA 1010-Ethyl Corp.) in 219g, 2.73 moles 2-chloroethanol, and heating to reflux in a three necked reactor vessel equipped with a reflux condenser, mechanical agitator and thermometer. The reaction was maintained at reflux for 5 hours until the starting tertiary amine was consumed (monitored by TLC). Unreacted chloroethanol was distilled off leaving a viscous brown residue which was shown to be the desired hydroxylated quaternary ammonium compound by proton magnetic resonance spectroscopy. The residual chloroethanol could be removed by wiped film evaporation to <<0.001% by capillary gas chromatrography. This synthesis may also be completed using epichlorohydrin instead of 2-chloroethanol.

EXAMPLE 2

The mTMI-quaternary ammonium carbamate was synthesized by dissolving 99.0g, (0.253 mole) of the hydroxylated quaternary ammonium compound in 150 ml dry toluene. 50.81g, (0.253 mole) m-isopropenyl-α'α dimethylbenzyl isocyanate (m-TMI) was added and brought to reflux. The reaction was catalyzed by addition of 3.0g (2% by weight) of potassium iodide-zinc acetate. After twenty-four hours a sample was withdrawn for IR and NMR analysis. Infra red analysis revealed a residual amount of isocyanate still present which was consumed by addition of a few drops of ethanolamine. Residual toluene was distilled off leaving

behind a viscous brown monomer. The structure of the desired quaternary ammonium carbonate adduct was confirmed by both proton NMR as well as, 13-C NMR spectroscopy.

EXAMPLE 3

Synthesis of m-TMI quaternary ammonium urea monomer was initiated by dissolving 153.8g 3- dimethylaminopropylamine, 1.50 moles, in 250 ml dry toluene and adding 302.5g (1.50 moles) m-TMI by dropwise addition over a sixty minute period at room temperature. The reaction mixture was brought to 70°C and the isocyanate concentration was monitored by IR spectroscopy. After 3 hours, the NCO was no longer detectable spectroscopically and the solvent was evaporated off under reduced pressure. Obtained 118.8g of the m-TMI tertiary amine adduct (73% of Theoretical) as a white crystalline solid. The structure was confirmed by proton NMR.

The tertiary amine adduct was quaternized by alkylation with bromododecane. 97.6g 1-bromododecane was dissolved in 200 ml toluene and 118.8g of the tertiary amine adduct was added and brought to reflux. The reaction mixture was monitored by TLC and observed consumption of the starting amine after six hours of reflux. Proton NMR analysis confirmed modification of the 3° amine to produce the desired alkylation product. This monomer was incorporated into an acrylic emulsion latex system.

EXAMPLE 4

The monomers formulated in Examples 2 and 3 were then used to synthesize the copolymers of Example 4. A hydroxyethylacrylate-quaternary ammonium carbamate copolymer was synthesized by dissolving 15g hydroxyethylacrylate and 15g of the quaternary ammonium carbamate in 60ml of isopropyl alcohol. 0.18g azobis-isobutyronitrile was added and reaction mixture was brought to 70°C for twenty-four hours and evaporated off the

isopropyl alcohol and unreacted hydroxyethylacrylate. A water soluble polymer preparation was obtained which was evaluated for antimicrobial activity and molecular weight.

A hydroxyethylacrylate-mTMI-Quat copolymer (70:30% by wt.) was analyzed by quasielastic laser light scattering. Molecular weights on this sample were obtained by calculation from the diffusion coefficient and radius of gyration measured. The diffusion coefficient $\bar{D}$ = 8.1 x 10^{-8} cm^2sec^{-1} with an observed radius of gyration = 25.0 nm. The calculated value of the weight average molecular weight = 42,380 g mole $^{-1}$.

A microbiological study was then run comparing a control, N-hydroxyethyl, N,N-methyl didecyl quaternary ammonium chloride with the polymer of Example 3 determine the minimal bactericidal concentration of a water soluble polymer over a 24 hour period.

The organisms shown in Table 1 were grown in tryptic-soy yeast extract (TSYE) broth for 24 hours. During growth the temperaure was maintained at 37°C in a shaking water bath.

The organisms were then spun down in sterile centrifuge tubes at 10,000 rpm for about five minutes and then decanted and resuspended in a phosphate buffer. The cells were then concentrated into one sterile centrifuge tube and spun down again, and the liquid was decanted. The cells were resuspended in five to ten mL of phosphate buffer, and spread on TSYE plates to determine the final concentration of cells. A final concentration of at least 1 x 10^6 in 10 mL was obtained for this experiment.

The amount of cells needed for the test was calculated in 10 mL of phosphate buffer. Dilutions of the polymer were made in tubes of sterile phosphate buffer for a final volume of 10 mL. The concentrations used to screen the polymer were 10, 100 and 200 ppm. The tubes were then

inoculated with the organisms at a concentration of 1 x 10^6 CFU/mL along with a control tube containing 10 mL of phosphate buffer and the organisms. A spread plate method was used to enumerate viable cells at zero time and 24 hours. The tubes were incubated in a 37°C shaking water bath during the 24 hour time period. The plates were incubated at 37°C for 48 hours. The plates were counted and converted to log values. Determination of logs of death in the polymer solution vs. the control were reported as minimum cidal concentration. Minimum cidal concentration is defined as the concentration of active ingredient necessary to provide greater than 5 log kill (CFU/ml) over a 24 hour period.

TABLE 1

MINIMUM CIDAL CONCENTRATION OVER 24 HOURS***

ORGANISM	CONTROL** (PPM)	EXAMPLE 3* (PPM)
L. monacytogenes (ATCC 1945)	1-10	10-50
S. typhi (ATCC 6539)	1-10	100-200
S. aureus (ATCC 6538)	1-10	200
C. albicans (ATCC 14053)	10-50	100-200
S. cervisiae (ATCC 9763)	1-10	10-50
E. coli (ATCC 1129)	10-50	200
P. aeruginosa (ATCC 15442)	10-50	600

***Assayed in presence of TSYE (1:1)

**N-hydroxyethyl, N, N-methyl didecyl quaternary ammonium chloride

*hydroxyethylacrylate: quaternary ammonium carbamate copolymer (70:30)

EXAMPLE 5

A latex emulsion containing the quaternary ammonium carbamate monomer was prepared by adding 31.1 wt-% of water and 0.1 wt-% of 0.05 molar sodium bicarbonate buffer to a jacketed and vented mixing vessel equipped with feed inlets. The charge was heated to 65°C under nitrogen purge. At 65°C, 0.15 wt-% each of ammonium persulfate and sodium metabisulfite as a catalyst was added and the monomer feed of, water (15.5 wt-%), surfactant (octylphenoxy polyethoxy ethanol 2.7 wt-%), methyl

methacrylate (23.4 wt-%), butyl acrylate (23.4 wt-%), methacrylic acid (0.7 wt-%), TMI/Quat monomer (2.5 wt-%), was then dripped in over a three and one-half hour time period. An additional 0.15 wt-% each of ammonium persulfate and sodium metabisulfate was added concurrent with the monomer addition. The reaction was held one hour at 65°C after all ingredients were added. The composition was then cooled and discharged into appropriate containers. The polymers of Example 4 were then subjected to microbiological testing to determine the ability of the polymers to resist attack from yeast and mold. The test involved a double challenge with sampling over a two week period.

Yeast and molds including A. niger (ATCC 9643), A. pullulans (ATCC 16622), P. funiculosum (ATCC 11797), C. albicans (ATCC 14053), and Saccharomyces cerevisiae (ATCC 9763) were used in the analysis.

Cultures of molds grown on agar slants which were at least two weeks old to insure the formation of spores were used. The yeast cultures grown on agar which were two to four days old were used. The original suspension of mold was scraped and resuspended and then diluted with the Tween 80 solution to yield a final spore count of 10 E5 per ml. The yeast cell count was determined with the use of the Prompt Inoculating System to yield a final cell count of 10 E8 per ml.

Fifty gram samples of the latex suspension were then transferred to two ounce bottles, and inoculated with 0.5 ml of the mixed inocula, mixed with a sterile tongue depressor and the bottles covered. The yeast and mold samples were determined separately so two samples of each adhesive was prepared, one for the yeast and one for the molds. The molds were incubated at room temperature and the yeast at 30°C.

Each sample was tested at 48 hours and one week. The samples were reinoculated as described above to repeat the testing. The plates were observed one week after they were streaked and scored according to the rating system described below.

Another analysis was initiated to determine the ability of a liquid sample to resist the growth of bacteria. The test assists in determining a system's inherent susceptibility to microbial attack prior to the addition of preservatives. The principle bacteria used in the analysis were P. aeruginosa (ATCC 15442), B. subtilis (ATCC 6051), and E. coli (ATCC 11229).

The Prompt Inoculating System (BBL, Becton Dickinson, Corp.) was used to prepare a bacterial inocula containing 1.8×10^8 colony forming units per ml. 50 g of the polymer was transferred to autoclaved two ounce bottles. Each sample was inoculated with 0.5 ml of each of the bacterial suspensions being careful to mix the suspension before sampling. The sample was mixed thoroughly with a sterile tongue depressor, covered and then incubated at 37°C.

Each sample was then tested at 48 hours and one week, reinoculated and repeatedly tested.

RESULTS

The sample with 2.5% (wt.) mTMI-Quat was susceptible to molds during the one month challenge test, but resistant to the bacterial and yeast inocula. The sample with 5% (wt.) mTMI-Quat was resistant to the molds, yeast and bacteria during the challenge period of one month.

EXAMPLE 6

An acrylonitrile quaternary ammonium copolymer was prepared by the aqueous dispersion technique discussed by Freshour and Knorr in Fiber Chemistry pp. 171-371 starting with a monomer solution was 90% acrylonitrile, 5% methyl acrylate and 5% mTMI-quaternary ammonium carbamate monomer by

weight. 100ml of water was blanketed with N_2 and brought to 58°C. The monomers were added to reaction vessel and polymerization was initiated by addition of 0.8g of 77ppm ammonium persulfate, 2.0g, 11.5% hydrogen peroxide and 3.0g 7% thiourea. The reaction mixture was agitated mechanically for 1 hour at 60°C during which time insoluble particles accumulated in suspension. Polymer chain propagation was quenched by addition of 1.0g of 8% EDTA at 90 minutes. Particulate polymer was washed with several volumes of water, filtered and air dried. The polyacrylonitrile-quaternary ammonium carbamate copolymer was soluble in dimethyl formamide. Filaments of this material were prepared by extrusion of the polymer dope, 8% (w/w), through an 18 gauge hypodermic needle into 5% aqueous dimethyl formamide bath at room temperature. Antimicrobial analysis of these filaments indicated that mold would not grow in their presence.

EXAMPLE 7

An mTMI-quaternary ammonium carbamate epoxy copolymer was prepared using 15g of isopropanol blanketed with N_2 and heated to 65°C, 0.20g azobis isobutyronitrile was dissolved. 5% of the termonomer mixture was charged into the reaction vessel: 12g (40%) mTMI-Quat, 16.5g (55%) Methyl methacrylate and 1.5g (5%) allylglycidyl ether.

After 18 hours at 65°C the volatiles were distilled off. Residual unreacted monomer was removed by extraction with 3 volumes hexane. A yellow viscous polymer preparation was obtained which by IR, exhibited evidence of ester at 1740 cm, oxirane groups at 1250cm and aliphatic ether at 1100cm.

Quantitation of the epoxy equivalent weight was accomplished by potassium iodide ring fission and tetration. An equivalent weight of about 2000g was observed.

The aforementioned epoxy resin was cured into a film with both a low molecular weight multifunctional amine, (Jeffamine D-400, available from Texaco), and a high molecular amine polyamide, (Versimide 140 available from Henkel). Cast films were cured at 200°F for 16 hours yielding tough adherent films with variable flexibility.

The films of Example 6 were tested for antibacterial activity against E. coli and found to promote a kill rate of greater than two log over 24 hours.

EXAMPLE 8

Synthesis of a water sensitive quat containing epoxy resin was initiated by charging a three necked round bottom flask with 12 g isopropanol and 0.18 g azobisisobutyronitrile and 2.0 g of the following monomer feed having 12.0 g mTMI-Quat (from Example 2), 16.5 g vinyl pyrrolidone, and 2.0 g allyl glycidyl ether.

The reaction vessel was brought to 65°C and blanketed with N_2. The monomer feed was commenced, and the temperature and agitation rate were held constant for 24 hours. The volatiles were distilled under reduced pressure and the polymer was extracted with three volumes of hexane. The polymer was found to have an equivalent weight of 2000, and was cured with the same amine epoxy curing agent as above.

Polyvinyl pyrrolidone-TMI-Quat-allylglycidyl ether terpolymer was observed to have a diffusion coefficient of 10.2×10^{-8} cm^2sec^{-1} with a radius of gyration = 19.9 nm which is equivalent to a $\bar{M}$-w = 21,370 g mole $^{-1}$.

Using the same protocol disclosed in the testing of Example 4, Example 7 was tested using the organism E. coli, (ATCC 11229). The sample was run using the concentrations 10, 100 and 200 ppm of the polymer. The logs of death at 0 time and 24 hours can be seen below.

Example 7	0 time	24 hours

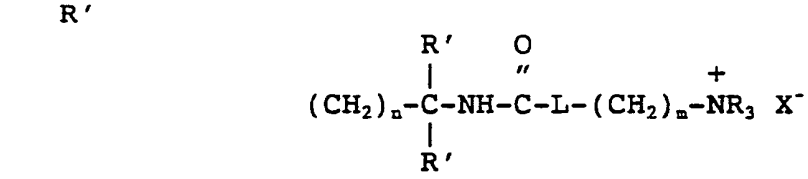
(ppm)		
10	4.32	>5.81
100	5.49	6.11
200	4.89	>5.81

The control solution having no polymer present was at 0 time = 7.49, and at 24 hours = 6.81. The sample was an effective biocide at 0 time and at 24 hours at all concentrations tested.

The foregoing specification, examples and data provide a basis for understanding the invention. The invention can be made in a variety of embodiments without departing from the spirit and scope of the invention. Accordingly, the invention resides in the claims hereinafter appended.

WHAT IS CLAIMED IS:

1. An antimicrobial copolymer composition, which comprises at least one vinyl monomer and up to about 99 mole-% of a second monomer of the formula:



wherein X^- is a halide; L is -O- or -NH-; n is 0-6, m is 1-6, each R′ is independently an H or C_{1-5} alkyl, and each R is independently a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl, or a benzyl group.

2. The copolymer of claim 1, wherein n is 0, m is 2, and R′ and at least two R substituents are methyl.

3. The copolymer of claim 2, wherein one R is a C_{8-10} alkyl.

4. The copolymer of claim 1, comprising from about 10 to 60 mole-% of the second monomer.

5. The copolymer of claim 1, wherein the vinyl monomer comprises an acrylic acid or methacrylic acid monomer.

6. The copolymer of claim 1, wherein the vinyl monomer comprises an acrylic acid ester or a methacrylic acid ester.

7. The copolymer of claim 1, wherein the vinyl monomer comprises a styrene, butadiene or mixtures thereof.

8. The copolymer of claim 1, wherein the vinyl monomer comprises a vinyl acetate.

9. The copolymer of claim 1, wherein the vinyl monomer comprises an alpha-olefin.

10. The copolymer of claim 1 wherein the vinyl monomer comprises a monomer having at least one epoxy functional group.

11. The copolymer of claim 1 wherein the vinyl monomer comprises an alkoxy silane.

12. The copolymer of claim 1 wherein the vinyl monomer comprises a perfluoroalkyl acrylate.

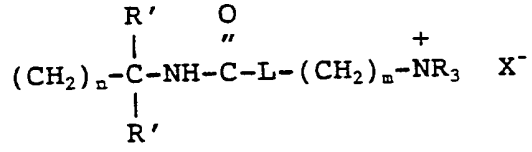
13. The copolymer of claim 1 wherein the vinyl monomer comprises a heterocyclic vinyl monomer.

14. The copolymer of claim 1, wherein the vinyl monomer is substantially free of acrylamide.

15. A film comprising a copolymer of claim 1.

16. A fiber comprising a copolymer of claim 1.

17. An aqueous copolymer latex having inherent antimicrobial action, which comprises a major proportion of water and dispersed therein a copolymer comprising a vinyl monomer and a second monomer of the formula:



wherein X^- is a halide; L comprises -O- or -NH-; n is 0-6, m is 1-6, each R′ is independently an H or C_{1-5} alkyl, and each R is independently a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl or benzyl group.

18. The aqueous copolymer latex of claim 17, wherein, in the second monomer, n is 0, m is 2, and at least two R substituents are methyl.

19. The aqueous copolymer latex of claim 18, wherein one R is a C_{8-10} alkyl.

20. The aqueous copolymer latex of claim 17, wherein the copolymer comprises from about 1 to 50 mole-% of the second monomer.

21. The aqueous copolymer latex of claim 17, wherein the latex comprises about 2 to 60 wt-%, of the copolymer.

22. The aqueous copolymer latex of claim 17, wherein the vinyl monomer comprises an acrylic and or methacrylic acid monomer.

23. The aqueous copolymer latex of claim 17, wherein the vinyl monomer comprises an acrylic acid ester or methacrylic acid ester.

24. The aqueous copolymer latex of claim 17, wherein the vinyl monomer comprises a styrene, butadiene, or mixtures thereof.

25. The aqueous copolymer latex of claim 17, wherein the vinyl monomer comprises vinyl acetate.

26. The aqueous copolymer latex of claim 17, wherein the vinyl monomer comprises an alpha-olefin.

27. The copolymer of claim 17 wherein the vinyl monomer comprises a monomer having at least one epoxy functional groups.

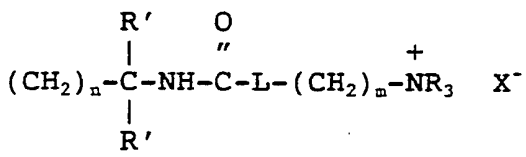
28. The copolymer of claim 17 wherein the vinyl monomer comprises an alkoxy silane.

29. The copolymer of claim 17 wherein the vinyl monomer comprises a perfluoroalkyl acrylate.

30. The copolymer of claim 17 wherein the vinyl monomer comprises a heterocyclic vinyl monomer.

31. The aqueous copolymer latex of claim 17, wherein the vinyl monomer is substantially free of acrylamide.

32. A solution copolymer having inherent antimicrobial action, which comprises a major portion of organic solvent and dissolved therein a copolymer comprising a vinyl monomer and a second monomer of the formula:



wherein X^- is a halide; L comprises -O- or -NH-; n is 0-6, m is 1-6, each R' is independently an H or C_{1-5} alkyl, and each R is independently a C_{1-24} alkyl, C_{1-24} alkyl substituted aryl or benzyl group.

33. The solution copolymer of claim 32 wherein in the second monomer, n is 0, m is 2, and at least two R substituents are methyl.

34. The solution copolymer of claim 33 wherein one R is a C_{8-10} alkyl.

35. The solution copolymer of claim 32 wherein the copolymer comprises from about 1 to 50 mole-% of the second monomer.

36. The solution copolymer of claim 32 wherein the latex comprises about 2 to 60 wt-%, of the copolymer.

37. The solution copolymer of claim 32 wherein the vinyl monomer comprises an acrylic and or methacrylic acid monomer.

38. The solution copolymer of claim 32 wherein the vinyl monomer comprises an acrylic acid ester or methacrylic acid ester.

39. The solution copolymer of claim 32 wherein the vinyl monomer comprises a styrene, butadiene, or mixtures thereof.

40. The solution copolymer of claim 32 wherein the vinyl monomer comprises vinyl acetate.

41. The solution copolymer of claim 32 wherein the vinyl monomer comprises an alpha-olefin.

42. The solution copolymer of claim 32 wherein the vinyl monomer comprises a monomer having at least one epoxy functional groups.

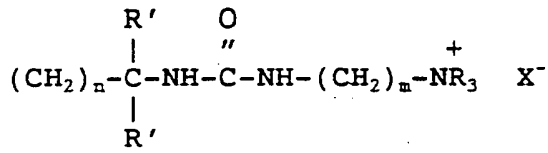
43. The solution copolymer of claim 32 wherein the vinyl monomer comprises an alkoxy silane.

44. The solution copolymer of claim 32 wherein the vinyl monomer comprises a perfluoroalkyl acrylate.

45. The solution copolymer of claim 32 wherein the vinyl monomer comprises a heterocyclic vinyl monomer.

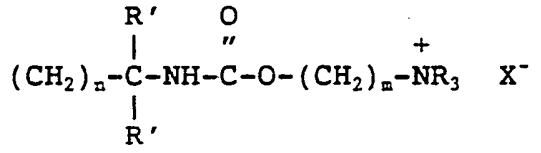
46. The solution copolymer of claim 32 wherein the vinyl monomer is substantially free of acrylamide.

47. An adhesive latex having inherent antimicrobial action, comprising water and dispersed therein a copolymer, wherein the copolymer comprises a vinyl monomer and at least about 1 mole-% of a second monomer of the formula:



wherein X^- is a halide; n is 0-6, m is 1-6, each R′ is independently an H or C_{1-5} alkyl, and each R is independently a C_{1-24} alkyl or a benzyl group.

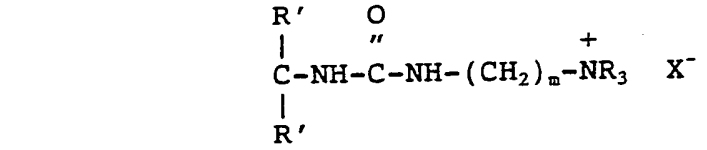
48. An adhesive latex having inherent antimicrobial action, comprising water and dispersed therein a copolymer, wherein the copolymer comprises a vinyl monomer and at least about 1 mole-% of a second monomer of the formula:



wherein X^- is a halide; n is 0-6, m is 1-6, each R′ is independently an H or C_{1-5} alkyl, and each R is independently a C_{1-24} alkyl or a benzyl group.

49. A copolymer having inherent antimicrobial action which comprises a hydroxyethyl acrylate monomer and about 1 to 50 mole-% of a second monomer of the formula:

R′

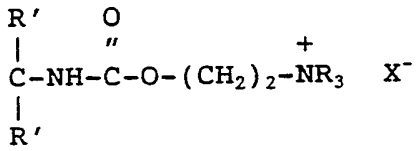


wherein X^- is a halide; R′ is independently an -H or a C_{1-5} alkyl, each R is independently a C_{1-24} alkyl or a benzyl, and at least two R are methyl.

50. The copolymer of claim 49, wherein one R is C_{8-10}.

51. A copolymer having inherent antimicrobial action which comprises a hydroxyethyl acrylate monomer and at least 1 mole-% of a second monomer of the formula:

R′

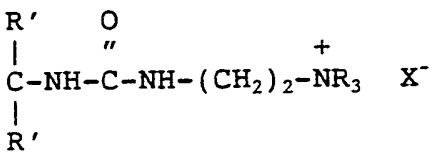


wherein R′ is independently an -H or a C_{1-5} alkyl, each R is independently a C_{1-24} alkyl or a benzyl, and at least two R are methyl.

52. The copolymer of claim 51, wherein one R is C_{8-10}.

53. A copolymer having inherent antimicrobial action which comprises styrene, butadiene or mixtures thereof and at least 1 mole-% of a second monomer of the formula:

R′

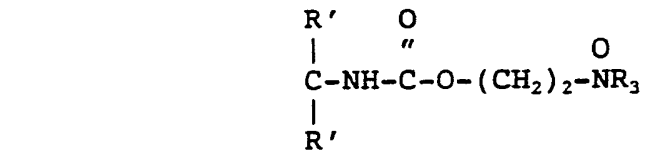


wherein R′ is independently an -H or a C_{1-5} alkyl, each R is independently a C_{1-24} alkyl or a benzyl, and at least two R are methyl.

54. The copolymer of claim 53, wherein one R is C_{8-10}.

55. A copolymer having inherent antimicrobial activity which comprises a styrene or butadiene monomer and at least 1 mole-%, of a second monomer of the formula:

R'



wherein R' is independently an -H or a C_{1-5} alkyl, each R is independently a C_{1-24} alkyl or a benzyl, and at least two R are methyl.

56. The copolymer of claim 55, wherein one R is C_{8-10}.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 91/00926

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC C 08 F 212/14,

IPC[5]: A 01 N 47/10, 47/28, C 07 C 271/12, 275/24

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	C 08 F, A 01 N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
A	US, A, 4429096 (F.C. SCHAEFER) 31 January 1984 cited in the application	
A	EP, A, 0169169 (SANDOZ PATENT) 22 January 1986	
A	US, A, 4532128 (B.G. SHELDON) 30 July 1985 cited in the application	

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
7th June 1991	01. 08. 91
International Searching Authority	Signature of Authorized Officer
EUROPEAN PATENT OFFICE	Nuria TORIBIO

Form PCT/ISA/210 (second sheet) (January 1985)

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. US 9100926
SA 45031

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on 16/07/91
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4429096	31-01-84	EP-A- 0127771	12-12-84
		JP-A- 59227854	21-12-84
EP-A- 0169169	22-01-86	AU-B- 590206	02-11-89
		AU-A- 4516885	23-01-86
		CA-A- 1247121	20-12-88
		JP-A- 61044846	04-03-86
		SU-A- 1402252	07-06-88
		US-A- 4968829	06-11-90
US-A- 4532128	30-07-85	EP-A- 0087473	07-09-83
		WO-A- 8301002	31-03-83
		US-A- 4482680	13-11-84

EPO FORM P0479

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82